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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,986

09/07/2006

Ryuji Ueno

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EXAMINER

THOMAS, TIMOTHY P

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

06/08/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,986	Applicant(s) UENO ET AL.	
	Examiner TIMOTHY P. THOMAS	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 March 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 11-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/20/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/9/2009 has been entered.

Election/Restrictions

2. Newly submitted claims 11-19 are directed to an invention that lacks unity with the invention originally claimed for the following reasons:

Group II (Claims 11-19), drawn to a method for increasing solubility, are placed into a separate invention group from the original claims, Group I (Claims 1-10), drawn to a composition. Groups I-II lack unity of invention because even though the inventions of these groups require the technical feature of a thiazole derivative of formula I and an additive, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of the prior art rejection presented below under 35 USC 103 (discussed in this Office Action and in prior Office Actions). Since the technical feature is rendered obvious by the prior art, the technical feature lacks inventive step; the technical feature is therefore not a special technical feature and the inventions are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-19 are withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

3. Applicants' arguments, filed 3/9/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

4. Applicant's arguments with respect to the rejection under 35 USC 103 have been fully considered but they are not persuasive:

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inoue, et al. (WO 2004/067521 A1; priority date 2003 Jan 27; IDS 3/30/2007 reference) and Ogata et al. (US 4,780,465; 1988); in view of Niebergall ("Ionic Solutions and Electrolytic Equilibria); 2000; "Remington: The Science and Practice of Pharmacy"; 20th Ed.; Gennaro, Ed.; Lippincott Williams & Wilkins; Chapter 17, pp. 227-245).

The teachings and motivations of Inoue and Ogata have been outlined on the record. Remington teaches the aqueous solubility of a slightly soluble organic substance generally is affected markedly by the addition of an electrolyte, an effect that is particularly noticeable when the electrolyte concentration reaches 0.5 M or higher, if the aqueous solution of the organic substance has a dielectric constant lower than that

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of pure water, its solubility is decreased and the substance is salted out (precipitated; p. 231, 2nd paragraph); the effect of electrolyte (KCl, KBr, NaCl and NaBr) on the salting out constant of a series of compounds related to and including barbital is shown in Table 17.3 (p. 231); in all instances, if the anion is constant, the sodium cation has a greater salting-out effect than the potassium cation, probably due to the higher charge density of the former, and for a constant cation, chloride anion has a greater effect than bromide anion upon the salting-out phenomenon (p. 231, 4th paragraph).

The salting out phenomena, taught by Niebergall, provides additional motivation to substitute an alternate isotonic compound, i.e., glycerin, mannitol or boric acid instead of the alternate NaCl taught by Ogata as isotonic agents. The recognition of the salting-out phenomenon provides motivation to exclude NaCl, and select an alternate non-salt isotonic agent, giving the compositions of the instant claims, within the scope of the "consisting essentially of" claim amendment, which applicant has argued, excludes NaCl based on disclosed data from Tables 1 and 2.

Applicant argues 1) with respect to the argument that the scope of the compound of the invention is quite different from Inoue, the present invention is a selection invention from the overall disclosure of Inoue and that the particular invention claimed in the present application provides unexpected results, a discussion which follows; 2) an advantageous property of Applicant's invention can be the subject of an argument for patentability without being recited in the claims; that additional claims have been added that specifically recite increasing solubility of the thiazole derivative of formula 1. It is noted that these claims are drawn to a non-elected invention group, and have been

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withdrawn. With respect to the advantageous property, demonstrated by unexpected results, the salting-out effect of salts such as KCl is well known in the art, as taught and demonstrated by Niebergall for barbital and related compounds. This phenomena at least qualitatively predicts the reduced solubility of the elected compounds in the presence of salts such as those disclosed in Tables 1 and 2. Additionally, the Tables disclose results for three compounds, none of which include the elected compound. Therefore, there are no unexpected results for the elected compound, which is under examination.

Applicant argues 3) the claims have been amended to the transitional language "consisting essentially of"; that in view of solubility shown in Table 1 this would be taken to exclude NaCl. The Niebergall teaching of salting out, specifically recognized as phenomenon that NaCl is causes, provides motivation to prepare solutions that contain an alternate isotonic agent, Such as one of those taught by Ogata.

Applicant argues 4) ionic compounds are now excluded from the claims because of the claim amendment changing "comprising" to "consisting essentially of"; such ionic compounds are excluded because they have a material effect on the basic and novel characteristics of the invention, as can be seen from Table 2. As discussed above, Niebergall provides motivation to choose a non-ionic compound as an isotonic agent.

Applicant further argues 5) the invention with "consisting essentially of" language provides unexpected results, including with respect to solubility and precipitation as shown in Tables 1 and 2, rebutting any prima facie case of obviousness. This argument is not persuasive. Experiments have been conducted with NaCl for 3 different

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compounds (Compounds A, B and C); two of which (A & C) demonstrate that at higher concentrations of NaCl precipitation occurs (Table 1). This behavior is considered expected, at least qualitatively, based on the salting-out phenomenon taught by Niebergall. Experiments have also been disclosed for a series of salts and non-salts with a single compound (Compound C), demonstrating higher solubility for glycerin, mannitol and boric acid, than for potassium chloride, disodium hydrogenphosphate or sodium citrate (Table 2). This result is also considered to be expected based on the salting out phenomenon for KCl and for Na salts taught by Niebergall. Additionally, the elected compound was not included in any of the experimental results; i.e., there is no unexpected result for the subject matter under examination. Therefore the rejection is maintained for the subject matter under examination, for which no unexpected results are of record.

Applicant argues that since Inoue does not even suggest the object of the present invention, i.e., preparing a clear and stable aqueous composition with the specific compound of the instant invention whose solubility in water will be decreased in the presence of an ionic component; that language directed to advantages does not need to be recited in the claims. The recognition of precipitation due to a salting-out effect, based on the teaching of Niebergall, is a specific recognition of this object; additionally teachings of aqueous parenteral solutions, imply that the compounds are/ should be soluble, taken with Niebergall leads to formulations that exclude salts that would lead to a salting-out effect.

5. Applicant's arguments, see pp. 10-11, filed 3/9/2009, with respect to the lined out IDS reference on the IDS filed 6/20/2008 have been fully considered and are persuasive. The English-language counterpart of the reference has been considered, as designated on the attached IDS sheet.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614